UNIVERSITÄT BIELEFELD
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Hierarchical organization of syntenic blocks in large genomic datasets

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Introduction

Synteny hierarchies for permutations

Synteny hierarchies for sequences

PSyCHO

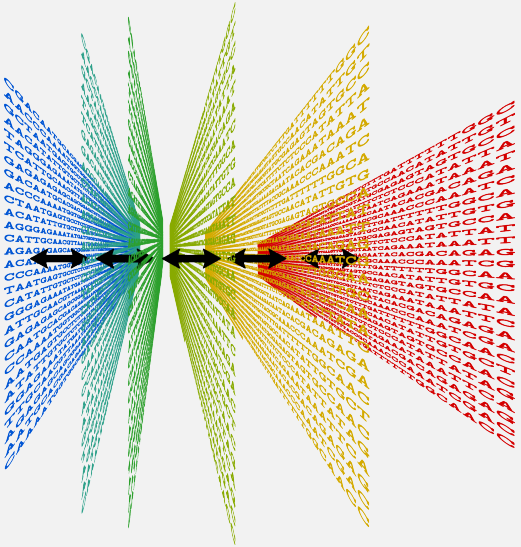
Data structures for large-scale comparisons

Objective:

- multi-species whole-genome comparisons

Solution:

- pan-genome data structures



Data structures for large-scale comparisons

Objective:

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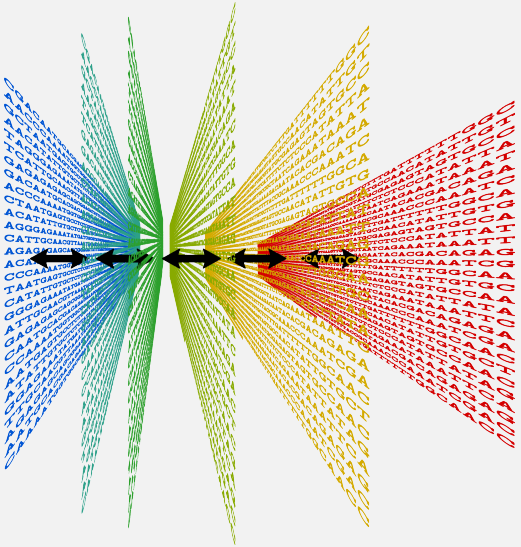
Solution:

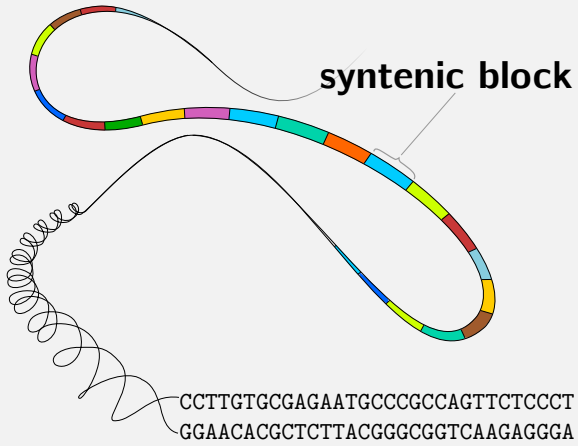
- pan-genome data structures

... only suitable for very similar genomes



Abstraction by decomposition

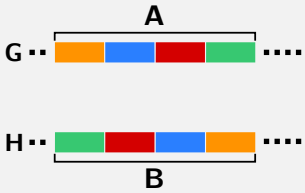
- genomes decomposed into *syntenic blocks*
- essential for studying genome evolution between distant species
  - current studies restricted to protein-coding genes
  - omission of many other conserved genomic regions



What is synteny?

A zoo of definitions:

- "*the same ribbon*" (Renwick, 1971) , set of markers co-located on same chromosome
- markers must be collinear
- local rearrangements allowed
- mostly tool-centric: FISH, GRIMM/DRIMM-Synteny, Cyntenator, i-ADHoRe, Sibelia, CoGe, Satsuma, *etc.*



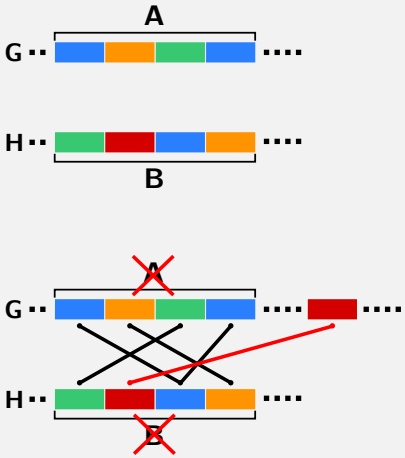
What is synteny?

homology assignment: set $\mathcal{H}$ of pairwise (equivalence) relations

Definition [Ghiurcuta and Moret, 2014]

Given two genomes G, H and homology assignment $\mathcal{H}$, two SBs $A \subseteq G$ and $B \subseteq H$ are homologous if for each

- $a \in A$: $\exists\,(a,h) \in \mathcal{H}, h \in H \implies (a,b') \in \mathcal{H}, b' \in B$
- $b \in B$: $\exists\,(b,g) \in \mathcal{H}, g \in G \implies (a',b) \in \mathcal{H}, a' \in A$



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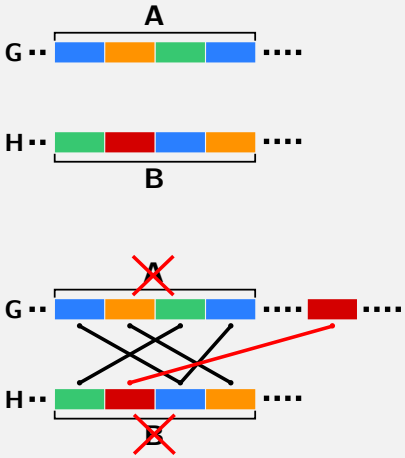
syntenic block (SB): single marker or set of contiguous syntenic blocks

dilemma:
there is no one true decomposition of genomes into syntenic blocks

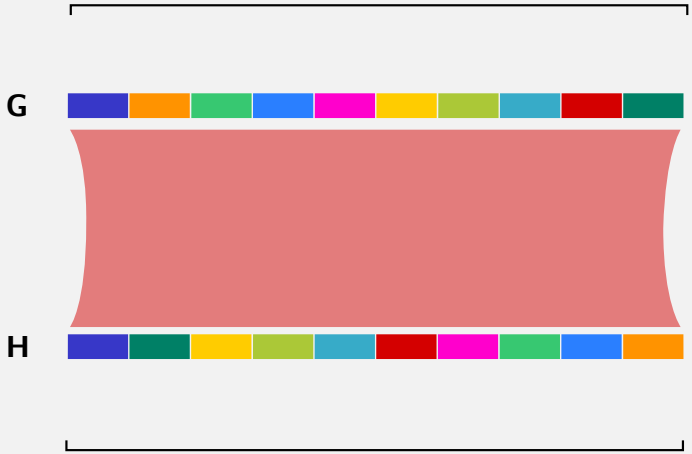


Synteny hierarchy

What are the homologous SBs of **G**,**H**?

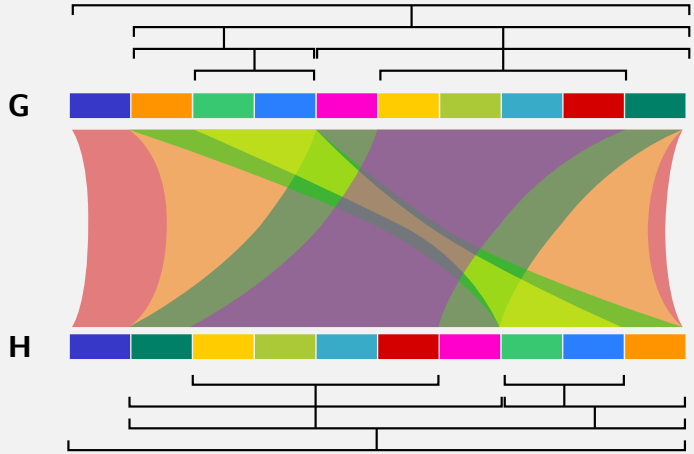
Synteny hierarchy

G, **H** are covered by one homologous SB pair



Synteny hierarchy

... but contains several other homologous SB pairs



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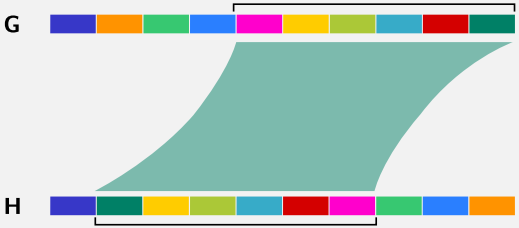
Common intervals in permutations

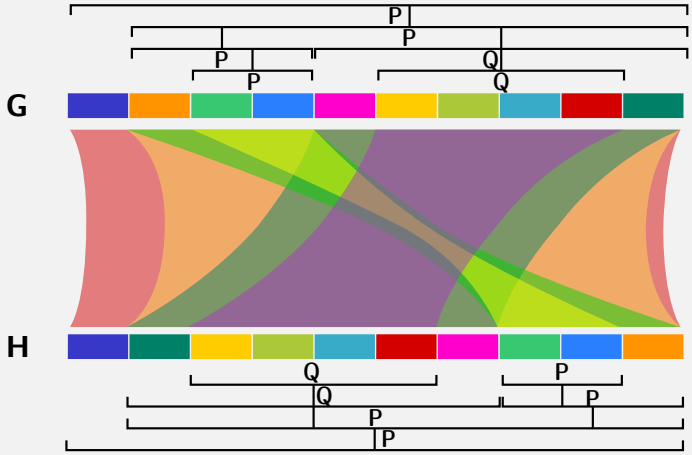
Definition

A pair of intervals of two permutations is *common* if they share the same set of elements.



Synteny hierarchy

PQ-tree: [Booth and Lueker, 1976] “**Q**”-node: collinear, “**P**”-node: permute freely



Booth and Lueker

PQ tree construction

linear time w.r.t. input size, i.e., number of 1s of an $n \times m$ matrix

- number of markers: n
- number of common intervals: $m \in O(n^2)$

... but cubic w.r.t. output size: the PQ tree has only $O(n)$ nodes!

Intervals of a PQ tree

Definition [Bergeron et al., 2008]

The *frontier* of a node is the set of labels of the leaves of the subtree rooted at this node, or a singleton comprising a leaf label.

Sets of common intervals in permutations

Definition [Bergeron et al., 2008]

A set of intervals $\mathcal{I}$ is *closed* if $(1), .., (n) \in \mathcal{I}$, $(1..m) \in \mathcal{I}$, and for each pair of intervals $(i..k), (j..l) \in \mathcal{I}$ s.t. $i < j \leq k < l$, also

$$(i..j), (j..k), (k..l), (i..l) \in \mathcal{I}$$

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Commuting sets

Definition [Bergeron et al., 2008]

Two intervals A, B commutes if

- $A \subseteq B$ or
- $B \subseteq A$ or
- $A \cap B = \emptyset$.

… and a set of intervals $\mathcal{I}$ is *commuting* if all pairs of intervals commute.

Strong intervals

Definition [Bergeron et al., 2008]

Given a set of intervals $\mathcal{I}$, an interval A is *strong* if it commutes with all intervals $B \in \mathcal{I}$.

The strong intervals of a closed set of intervals $\mathcal{I}$ are the frontier of the PQ tree of $\mathcal{I}$.

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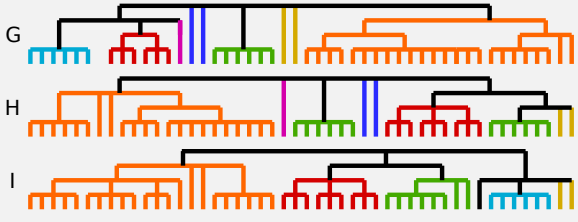
SB hierarchy

Context-dependency

two sets of common intervals intersect *only* if all their intervals intersect in the corresponding sequences



Sets of common intervals in sequences

Definition

A set of intervals $\mathcal{I}$ is *near-closed* if $(1), .., (n) \in \mathcal{I}$, $(1..m) \in \mathcal{I}$, and for each pair of intervals $(i..k), (j..l) \in \mathcal{I}$ s.t. $i < j \leq k < l$, also

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Sets of common intervals in sequences

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A set of intervals $\mathcal{I}$ is *near-closed* if $(1), .., (n) \in \mathcal{I}$, $(1..m) \in \mathcal{I}$, and for each pair of intervals $(i..k), (j..l) \in \mathcal{I}$ s.t. $i < j \leq k < l$, also

$$(i..l) \in \mathcal{I}$$

Lemma

Let $\mathcal{I}$ be a near-closed set of intervals. Then there exists a unique *PQ*-tree with frontier $\mathcal{F}$ such that for the set of strong intervals $I' \subseteq I$ holds true that $\mathcal{I}' \subseteq \mathcal{F}$ and $|\mathcal{I}| \geq \lceil 1/2 \cdot |\mathcal{F}| \rceil$.

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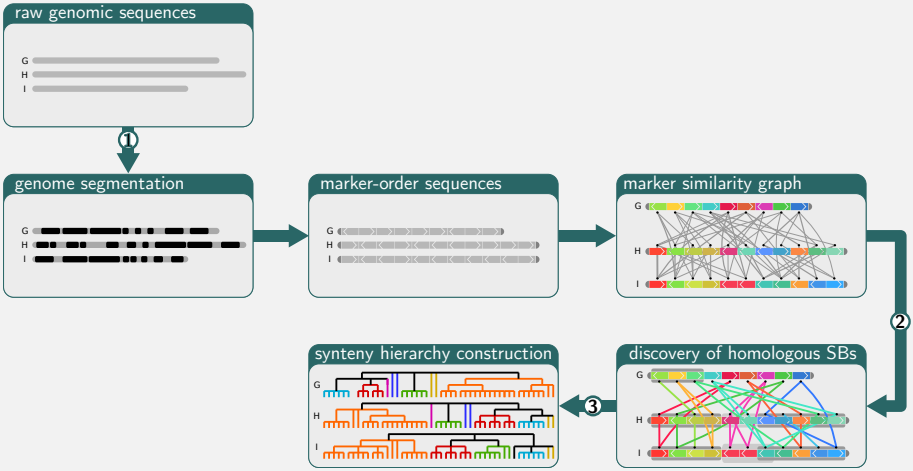
PSyCHO

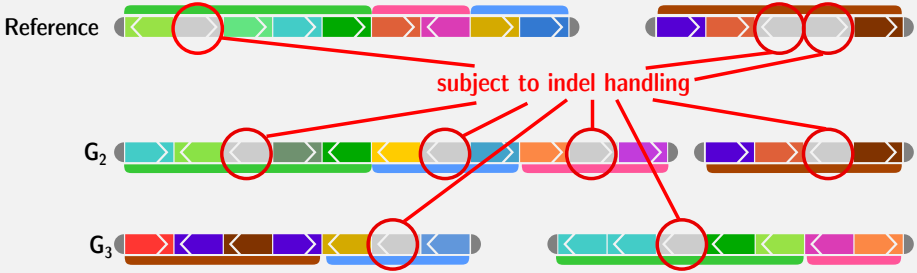
Principled Synteny using Common Intervals and Hierarchical Organization

`http://github.com/danydoerr/PSyCHO`

Construction of a synteny hierarchy

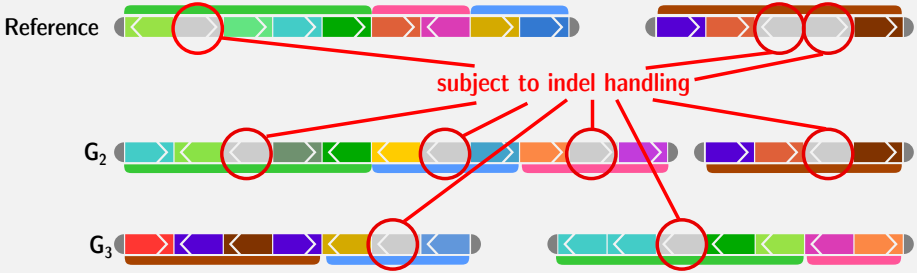


Similarity graph, syntenic contexts, homologous SBs



1. reference-based reconstruction of syntenic contexts
   - computational problem: finding δ-teams in sequences

Similarity graph, syntenic contexts, homologous SBs



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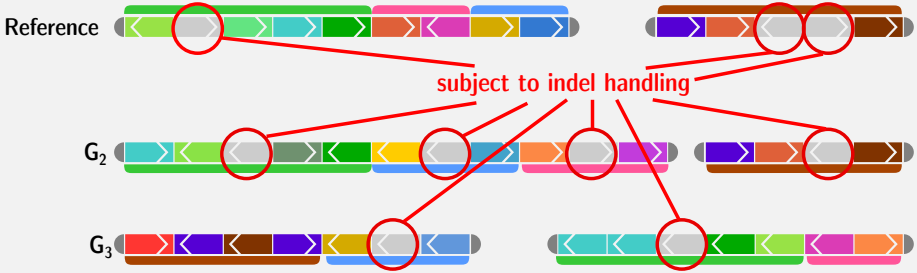
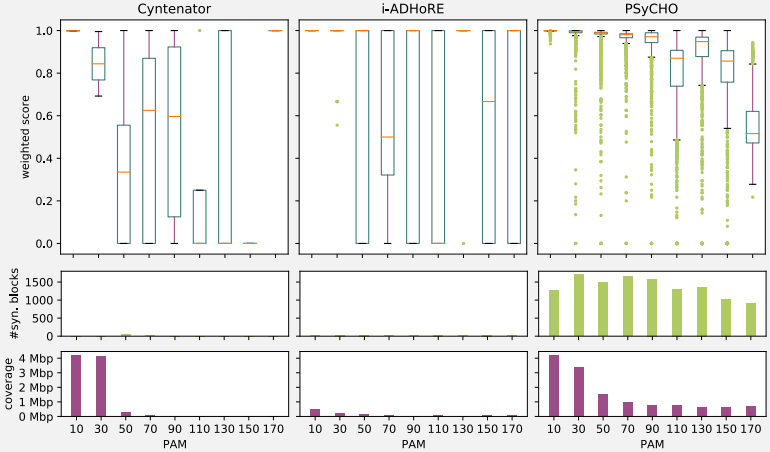
Similarity graph, syntenic contexts, homologous SBs



1. reference-based reconstruction of syntenic contexts
   - computational problem: finding δ-teams in sequences
2. handling of insertions/deletions *(work in progress)*
3. reference-based discovery of homologous syntenic blocks in each context
   - computational problem: enumerating common intervals in k sequences

Analysis of simulated genomes

5 species, 1000 markers of length 300,
point mutations+rearrangements+ins+del+dupl



Analysis of simulated genomes

Weighted Synteny Score: Fraction of markers in a homologous set of syntenic blocks that have at least one homologous counterpart in each block or have no homologous counterpart at all in the respective genomes.

Analysis of simulated genomes

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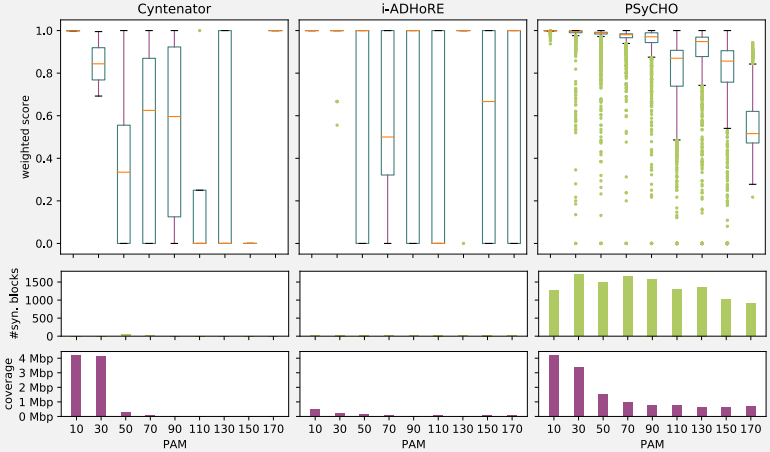
point mutations+rearrangements+ins+del+dupl



Analysis of Drosophila genomes

species	ID	scaffolds	size (Mbp)	CDSs	markers
D. *melanogaster*	D.mel	7	120.3	30,443	98,214
D. *simulans*	D.sim	6	118.2	24,119	100,549
D. *yakuba*	D.yak	6	119.5	23,304	100,774

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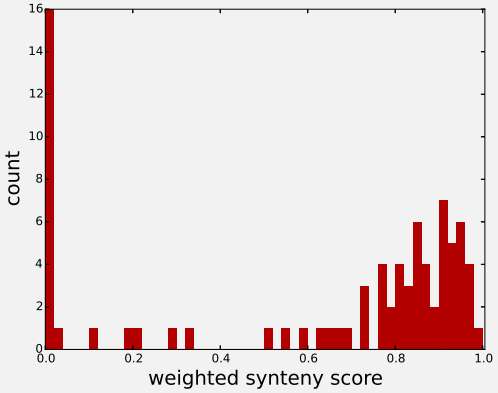
Analysis of Drosophila genomes

	genome	PSyCHO	i-ADHoRe
coverage	D.mel	**0.782**	0.682
	D.mel	0.823	**0.840**
	D.yak	**0.783**	0.763
#SBs		top: 10 int. nodes: 2090	80

Weighted Synteny Score [Ghiurcuta and Moret, 2014]

i-ADHoRe



PSyCHO: 1 (by def.)

Thank you!

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